UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,995	10/05/2001	John P. McKearn	CU-2560 RJS	4037

7590 03/18/2004

Mr. James M. Warner
Assistant General Counsel
Pharmacia Corporation, Global Patent Department
800 North Lindbergh Blvd.
St. Louis, MO 63167

EXAMINER	
PATEL, SUDHAKER B	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 03/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/857,995	MCKEARN ET AL.	
	Examiner	Art Unit	
	Sudhaker B. Patel, D.Sc.Tech.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 1934*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,11,21,43-46,54,71,86,87,107,108 and 110-133* is/are pending in the application.

4a) Of the above claim(s) *4-10,12-20,22-42,47-53,55-70,72-85,88-106,109* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,43,44,86,87,107 and 108* is/are rejected.

7)☐ Claim(s) *2,3,11,21,45,46,54,71 and 110-133* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/21/04;#24*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' communication paper dated 2/12/04 is acknowledged. Together with their earlier communication(s), applicants have cancelled claims 4-10,12-20,22-42,47-53,55-70,72-85,88-106,109, amended claims 1,2,3,44,45,46,107,108, and added new claims 110-133. Therefore, the claims in this application are the claims 1-3,11,21,43-46,54,71,86-87,107-108,110-133. Applicants' arguments and remarks have been reviewed, and after further consideration found not persuasive for allowance of this application for following reasons.

Rejections withdrawn/maintained: (I). The rejections stated under 35 U.S.C. 112 paragraph fisrt related to "prevention" of a diseases are withdrawn. However the rejections for treating a specific neoplasms are maintained for the reasons stated bellow.

(2). The rejections made under 35 U.S. 103(a) against references except ref. Zook et al (WO 9720824) are withdrawn. I.e. Ref. '583, '343, '685. See rejections bellow

Election/Restrictions

Applicants' have elected invention of Group I and species of Compound # 11 and claims (in part) 1-3,11,21,43-46,54,71,86-87,107-108,110-133. The restriction/election is considered proper and is now made FINAL.

New Rejections:

Claim Rejections - 35 USC § 103

1. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claim1, 43,107,44,86,87,108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zook et al (WO97220824 dated 6/12/01996) as applied to claims above, and further in view of Anderson et al (Seminars in Oncology, 23/5, Supplement 11,46-56(1996) also cited as Chemical Abstract DN125: 316004).

3. Zook et al teaches applicants' heterocyclic metalloproteinase-inhibitor (MMP) and its utility for inhibition of lung metastases, also as antitumors as claimed herein. See the compounds with CAS RN # 192330-51-1; 192329-42-3; 192329-58-1; 192330-53-3; all of which have a basic core:" Pyridine-O-phenyl-SO2- dimethyl-thiomorpholine-CO-NH-OH.

4. Anderson et al teaches combinations of active antineoplatic agents e.g. paclitaxel with established antineoplastic drugs for breast cancer radiation therapy as well as novel investigational agents or strategies.

5. The references do not teach the combination together. Accordingly, one skilled in this art would fins ample motivation from the prior art(s) supra to combine the well known anti-cancer therapies together, where the results obtained thereby are no more than the additive effects of the ingredients. See In re Sussman, 1943 C.D. 518. The specification fails to set forth data showing a greater than additive effect for the claimed combination. Claims directed to a showing of greater than additive effect would overcome this rejection.

6. Claims rejected under 35 U.S.C. 103(a) as being unpatentable over Relias et al(Chemical abstract DN 128:212465 also cited as J. Oncology Pharmacy Practice ¾,173-185(1997)).

7. Relias teaches inhibitor Topotecan and its use in treating lung and ovarian cancer, radiation sensitization.

8. The reference Relias does not teach the combination together. However, one skilled in this art would find ample motivation from the prior art(s) supra to combine the well known anti-cancer therapies together, where the results obtained thereby are no more than the additive effects of the ingredients. See In re Sussman, 1943 C.D. 518. The specification fails to set forth data showing a greater than additive effect for the claimed combination. Claims directed to a showing of greater than additive effect would overcome this rejection.

9. Claims 1,43,44,86 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific neoplasis related to a specific lung disorder, does not reasonably provide enablement for the term"neoplasis disorder" defined to include more than 80 different disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to practice the invention commensurate in scope with these claims. The term neoplasia as defined lacks clear exemplary support in the specification as filed.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546(MPEP 2164.01(a)). The factors include: **1)**. The nature of the invention, **2)**. the state of the prior art, **3).** the predictability or lack thereof in the art, **4).** the amount of direction or guidance present, **5)**. the presence or absence of working examples, **6).** the breadth of the claims, and **7).** the quantity of experimentation needed.

1) The nature of the invention: The method of use claims are drawn not only to treating a specific neoplasia disorder but treating neoplasia disorder broadly with a single MMP and antineoplastic agent selected from the group consisting of irinotecan and topotecan and a combination thereof with and without radiation therapy in a mammal. Thus, the claims are not limited to simple combination but also to complex 3- or more variables/components to treat more than 80 disorders as claimed herein.

2) The state of the prior art: While the state of the art is relatively high with regard to treatment of specific cancers, the state of art with regard to treating cancer(s) or neoplasms broadly is underdeveloped. In particular there is no known anticancer agent, which is effective against all cancers. The Carter et al reference clearly teaches that for the forty known anticancer agents, none are effective against all cancers. (See pages 362-365 of Carter et al reference).

3) The predictability or lack thereof in the art: It is presumed in the treatment of the diseases claimed herein there is a way of identifying any and all of the diseases which are responsive to the activity of MMP, Antineoplastic agent, and radiation without unexpected and serious toxic effects observed. The lack of significant guidance from the specification or prior art(s) with regard to the actual treatment of all cancers or neoplasms in a mammal including humans subject with the claimed combination makes practicing the claimed invention unpredictable.

4) The amount of direction or guidance present and 5) the presence or absence of working examples: There are no doses present for the treatment of the disorders recited. The guidance given by the specification as to how one would administer the claimed combination(s) to a mammal in order to treating neoplasms broadly. The guidance provided by the specification is directed to specific cancer. See Table in page 217 lines 12-15, which recites Pancreatic Cell (PC-3) Model MMP inhibitor Combination Study Results with COMPOUND M 14 and not with the elected species of Compound 11, which is a different chemical/structure. The model does not include either irinotecan or topotecan as claimed herein. Similar are the stated results in Tables as recited in other models wherein only Compound 14 is recited. See Table in page 218 lines 15-end of the page. Tables in page 219 lines 1-3 and in lines 11-end of page, Table in page 220 lines 13-15 Table in page 221 I lines 10-13. Only Table in page 222 lines 1-5 recite use of Irinotecan with compound 14 only, and there is no mention of elected species of Compound # 11.All the working examples provided by specification are directed to specific cancers.

6) The breadth of the claims: The claims are drawn to disorders that are not related and whose treatment is unknown. Thus, the complex nature of the claims greatly

exacerbated by breadth of the claims. The claims encompass treating neoplasms broadly in a mammal.
7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Applicants fail to provide guidance and information to allow the skilled artisan to ascertain which particular type of cancer the claimed antineoplastic agents are effective against without undue experimentation. The limited disclosure of several cancers is noted but will not support all cancers being claimed. The Carter at el reference shows data on 23 types of cancer. Applicants should at least test these types of cancer with claimed anticancer agents in combination with/without radiation therapies.

Claim Objections

10. Claims 2,3,11,21,45,46,54,71 are objected to because of the following informalities: They are dependent on rejected claims, in particularly claim 71 limits claim 44 to only 9 different cancers. Appropriate correction to actual results obtained for a specific cancer(s) is required.

Allowable Subject Matter

11. Claims 110-133 are objected to as being dependent upon a rejected base claims, but would be allowable if rewritten in independent form to limit the cancer(s) for actually tested for the elected invention of Group I and species of Compound # 11 only, including all of the limitations of the base claims, and overcoming the rejections as stated above and any intervening claims.
12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhaker B. Patel, D.Sc.Tech. whose telephone number is (571) 272-0671.

The examiner can normally be reached on 6:30 to 5:00 pm (Monday-Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund J. Shah can be reached on (571) 272 0674 or Sr. Examiner Mr. Richard Raymond at (571) 272 0673 or Mr. James Wilson at (571) 272-0661.

The assigned centralized fax number for the organization/USPTO for processing of this application or its proceedings is (703)–872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1235.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sudhaker B. Patel, D.Sc. Tech.
March 15, 2004.

MUKUND SHAH
SUPERVISORY PATENT EXAMINER
ART UNIT 1624